C1 canceled

relative amounts such that when a therapeutic amount is applied to the skin a minimal systemic effect is produced.

REMARKS

I. Status of the Claims

Claims 24, 25, and 28-39 are pending in this application. Claim 26 has been canceled. Claim 24 has been amended to clarify the scope of the claim. No new matter has been introduced by this amendment, nor does this amendment necessitate any additional search by the Office.

Applicants acknowledge and appreciate that the rejections under 35 U.S.C. § 112, first and second paragraph, have been withdrawn by the Examiner. *See* Final Office Action dated March 12, 2002, page 2. Applicants further acknowledge and appreciate that the rejection of claims 24-26 and 28-39 under 35 U.S.C. § 103(a) over U.S. Patent 5,648,389 to *Gans et al.* ("*Gans*") has also been withdrawn. *See* Final Office Action dated March 12, 2002, page 3.

II. Request to Withdraw Finality

The Office Action dated March 12, 2002, was made final by the Examiner. Applicants respectfully disagree and believe that the finality of the March 12, 2002, Office Action is improper because the Office Action contains two new grounds of rejection. Specifically, claims 24, 25, 28, 30-34 and 36-39 were newly rejected under 35 U.S.C. § 102(a) over U.S. Patent Application Publication No. US 2001/0031769 to

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HENDERSON
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1300 I Street, NW
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202.408.4000
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Jackman et al. ("*Jackman*") and claims 24-26 and 28-39 were newly rejected under 35 U.S.C. § 103(a) over *Gans* in view of *Jackman*.

The Manual of Patent Examining Procedure ("the *MPEP*") specifies that a second or subsequent action on the merits shall be made final *except* where the examiner introduces a new ground of rejection that is not "necessitated by applicant's amendment." M.P.E.P. § 706.07(a). In the present case, the new ground of rejection was not necessitated by amendment, nor does the Examiner allege that it was. *See* pages 3-4 of the Final Office Action dated March 12, 2002. Accordingly, Applicants respectfully submit that the finality of this Office Action is improper and request that the finality be withdrawn.

III. Rejection Under 35 U.S.C. § 102(a)

The Examiner has rejected claims 24, 25, 28, 30-34, and 36-39 as anticipated under 35 U.S.C. § 102(a) by U.S. Patent Application Publication No. US 2001/0031769 to *Jackman et al.* ("*Jackman*"). Applicants respectfully traverse this rejection.

As a preliminary matter, Applicants note that the cited reference is not proper prior art under 35 U.S.C. § 102(a). To properly apply 35 U.S.C. § 102(a) against the instant application, "the reference must have a publication date earlier in time than the effective filing date of the application, and must not be applicant's own work." M.P.E.P. § 706.02(a)(III). The effective filing date of the instant application is the filing date of the international application, which is November 5, 1998. M.P.E.P. § 1893.03(b). The cited reference, however, bears a publication date of October 18, 2001, which is later in time

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than the effective filing date of the instant application. Thus, *Jackman* is not prior art under 35 U.S.C. § 102(a).

Applicants recognize, however, that *Jackman* has an international counterpart, International Publication No. WO 96/13249, which was published May 9, 1996. As the publication date of WO 96/13249 is earlier in time than Applicants' priority date, which is November 7, 1997, this reference could qualify as a reference under 35 U.S.C. § 102(a). Although the Examiner has not cited WO 96/13249 against the instant application, Applicants recognize that the Examiner could have cited, or could still cite, *Jackman* as an equivalent thereof. Accordingly, Applicants below address the merits of the rejection over *Jackman*.

To anticipate the present claims successfully, a reference must show the "identical" invention "in as complete detail as is contained in the ... claim[s]." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 U.S.P.Q.2d 1913, 1920 (Fed. Cir. 1989). Further, without the need for picking, choosing, and combining various disclosures, the reference must direct those skilled in the art to the invention. *In re Arkley*, 455 F.2d 586, 587, 172 U.S.P.Q. 524, 526 (C.C.P.A. 1972). *Jackman* does not fulfill these requirements.

Jackman does not teach every element of at least Applicants' claim 24 clearly and unequivocally. For example, claim 24 of the instant invention recites that the components of the formulation "are present in relative amounts such that when a therapeutic amount is applied to the skin a minimal systemic effect is produced." *Jackman*, however, fails to discuss anything with respect to minimizing the systemic

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effect of an immunosuppressive macrolide. *Jackman* discloses sorbic acid, which is an alkenoic acid. But *Jackman* teaches sorbic acid, not as a permeation modulator, but as a preserving agent, preferably, in an amount of about 0.01% to about 2.5%. (*Jackman*, paragraph [0058].) Generically, it also teaches organic acids, including sorbic acid, in an amount of up to 5% by weight. (*Jackman*, paragraphs [0073] and [0078].) The reference does not, however, teach any relationship between its immunosuppressive macrolide and its alkenoic acid. And the reference fails to teach that, by altering the relative amounts of its immunosuppressive macrolide and its alkenoic acid in composition, the systemic effect of the macrolide can likewise be adjusted. Thus, Applicants' invention is not clearly and unequivocally taught by *Jackman*.

Additionally, Applicants note that the Examiner has rejected claim 36, which recites that "the solvent system is 5% to 90% by weight." In order for an anticipation rejection to be proper, "each and every element as set forth in the claim" must be expressly or inherently described in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). Although the Examiner has pointed to paragraph [0058] of the reference for teaching benzyl alcohol, this disclosure also provides that benzyl alcohol is intended as a preserving agent, in an amount of about 0.01 to about 2.5%. And, in the examples, benzyl alcohol is not present in an amount more than 1% by weight. Thus, *Jackman* fails to teach a solvent system in an amount of 5% to 90% by weight. *Jackman*, therefore, fails to teach each and every element of claim 36.

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Thus, because *Jackman* does not teach all the elements of Applicants' claims clearly and unequivocally, it fails to anticipate Applicants' claims. Accordingly, Applicants respectfully request withdrawal of this anticipation rejection.

IV. Rejection Under 35 U.S.C. § 103(a)

The Examiner has rejected as obvious claims 24-26 and 28-39 as unpatentable under 35 U.S.C. § 103(a) over *Gans* in view of *Jackman*. (Final Office Action dated March 12, 2002, pages 3-5.) The Examiner alleges that it would have been obvious to use the components taught by *Jackman* in the invention of *Gans* to obtain a functionally equivalent composition. (Final Office Action dated March 12, 2002, page 5, lines 3-5.) Applicants respectfully traverse this rejection for at least the following reasons.

To establish a *prima facie* case of obviousness the Examiner must at least show that all of the claimed elements are taught or suggested by the cited references. M.P.E.P. § 2143. As is discussed above, with respect to the 35 U.S.C. § 102 rejection, *Jackman* fails at least to teach that the components of the formulation "are present in relative amounts such that when a therapeutic amount is applied to the skin a minimal systemic effect is produced," and *Gans* does not remedy this deficiency. For example, *Gans* teaches caprylic acid, not as a permeation modulator, but as a choice for the reference's antimicrobial, antibiotic, antibacterial, or antifungal agent. (*Gans*, col. 2, lines 42-57.) And, although *Gans* discloses generally that combinations of antimicrobial, antibiotic, antibacterial, or antifungal agents may also be used, the reference does not teach the combination of any of the claimed antibiotics with a permeation modulator, let alone these two components "in relative amounts such that

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when a therapeutic amount is applied to the skin a minimal systemic effect is produced." Further, for example, not one of *Gans'* examples even discloses such a combination. Thus, neither reference individually nor in combination teaches all of the elements of Applicants' claims, as is required for a *prima facie* case of obviousness.

Further, when relying on a combination of references, to establish a *prima facie* case of obviousness the Examiner must show some teaching, suggestion or incentive supporting the combination of reference teachings. *In re Geiger*, 815 F.2d 686, 688 (Fed. Cir. 1987) (citation omitted). "The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." M.P.E.P. § 2143.01 (emphasis in original and emphasis supplied). Here, the Examiner has not shown why one of ordinary skill in the art would have had the incentive to make the proposed combination.

The Examiner reasons that incentive to combine the reference teachings lies in the expectation of enhancing the *Gans* composition by adding the materials of *Jackman* to treat additional diseases as disclosed by *Jackman*. (Final Office Action dated March 12, 2002, page 5, lines 1-2.) But the Examiner has failed to consider the effect that one of the required "materials" of *Jackman*, the unsaturated fatty alcohol, would have on the combination. Accordingly, Applicants respectfully submit that this rejection is improper because "[i]t is impermissible within the framework of § 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to

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one of ordinary skill in the art." *In re Wesslau*, 353 F.2d 238, 241, 147 U.S.P.Q. 391, 393 (C.C.P.A. 1965).

Specifically, *Jackman* teaches an emulsion comprising: (1) a compound of the FK506 class, (2) a specific solvent, (3) an unsaturated fatty alcohol, and (4) water. (*See Jackman*, Abstract.) Further, *Jackman* discloses that "[t]he composition preferably contains sufficient amounts of the unsaturated fatty alcohol to promote absorption of the compound of the FK506 class in the skin." (*Jackman*, page 2, paragraph [0034] (emphasis supplied).) In contrast, Applicants' claim 24 provides that the macrolide and the permeation modulator are present "in relative amounts such that when a therapeutic amount is applied to the skin a minimal systemic effect is produced." The permeation modulator of the instant invention provides for partial penetration of the skin to avoid "significant absorption of the [macrolides] into the systemic circulation." (Specification, page 5, lines 11-33.) In fact, the instant specification provides a distinction between permeation enhancers, which are used to increase the drug flux across the skin, and permeation modulators, which allow penetration of the skin without significant passing through the epidermis into systemic systems. (Specification, page 3, lines 3-11.) Thus, once all of the relevant teachings of the references are considered, it is clear that the proposed combination does not teach or suggest the instant invention.

Accordingly, Applicants respectfully submit that the rejection under § 103 is improper and respectfully request its withdrawal.

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V. Conclusion

In view of the foregoing amendment and remarks, Applicants respectfully request the reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: September 10, 2002

By: _____
Michele L. Mayberry
Reg. No. 45,644

Attachment: Appendix

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HENDERSON
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1300 I Street, NW
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ATTENTION: BOX AFTER FINAL
AMENDMENT AND REPLY AFTER FINAL REJECTION UNDER 37 C.F.R. § 1.116
EXPEDITED PROCEDURE REQUESTED
EXAMINING GROUP 1616

Application No. 09/530,375
Attorney Docket No. 1142.0236-00
Customer No. 22,852

APPENDIX TO AMENDMENT

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Please cancel claim 26 and amend claim 24 as follows:

24. (Twice Amended) A topical formulation for the treatment of a dermatological condition which comprises ~~a macrocyclic lactone antibiotic, an immunosuppressive macrolide wherein the macrolide is~~ **a macrocyclic lactone antibiotic chosen from azithromycin or clarithromycin or an immunosuppressiv macrolide chosen from** sirolimus, FK506 or SDZ ASM 981, and a permeation modulator which are present in relative amounts such that when a therapeutic amount is applied to the skin a minimal systemic effect is produced.

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PATENT
Customer No. 22,852
Attorney Docket No. 01142.0236-00

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	)	
Anthony ORMEROD et al.	)	Group Art Unit: 1616
	)	
Application No.: 09/530,375	)	Examiner: M. Williamson
	)	
Filed: July 7, 2000	)	
	)	
For: SKIN PENETRATION ENHANCING COMPONENTS	)	
	)	

Commissioner for Patents
Washington, DC 20231

Sir:

REVOCATION OF POWER OF ATTORNEY
AND GRANT OF NEW POWER OF ATTORNEY

The undersigned, a representative authorized to sign on behalf of the assignee owning all of the interest in this patent, hereby revokes all previous powers of attorney or authorization of agent granted in this application before the date of execution hereof. The undersigned verifies that Wyeth is the assignee of the entire right, title, and interest in the patent application identified above by virtue of an assignment from the inventors to Aberdeen University recorded in the U.S. Patent and Trademark Office on July 7, 2000, at Reel 010953, Frame 0804 and an assignment from Aberdeen University to Wyeth executed on August 7, 2002, and August 28, 2002, and filed together herewith.

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1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

The undersigned certifies that the evidentiary documents have been reviewed and to the best of the undersigned's knowledge and belief, title is in the assignee Wyeth.

The undersigned hereby grants its power of attorney to **FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P.,** Douglas B. Henderson, Reg. No. 20,291; Ford F. Farabow, Jr., Reg. No. 20,630; Arthur S. Garrett, Reg. No. 20,338; Donald R. Dunner, Reg. No. 19,073; Brian G. Brunsvold, Reg. No. 22,593; Tipton D. Jennings, IV, Reg. No. 20,645; Jerry D. Voight, Reg. No. 23,020; Laurence R. Hefter, Reg. No. 20,827; Kenneth E. Payne, Reg. No. 23,098; Herbert H. Mintz, Reg. No. 26,691; C. Larry O'Rourke, Reg. No. 26,014; Albert J. Santorelli, Reg. No. 22,610; Michael C. Elmer, Reg. No. 25,857; Richard H. Smith, Reg. No. 20,609; Stephen L. Peterson, Reg. No. 26,325; John M. Romary, Reg. No. 26,331; Bruce C. Zotter, Reg. No. 27,680; Dennis P. O'Reilley, Reg. No. 27,932; Allen M. Sokal, Reg. No. 26,695; Robert D. Bajefsky, Reg. No. 25,387; Richard L. Stroup, Reg. No. 28,478; David W. Hill, Reg. No. 28,220; Thomas L. Irving, Reg. No. 28,619; Charles E. Lipsey, Reg. No. 28,165; Thomas W. Winland, Reg. No. 27,605; Basil J. Lewris, Reg. No. 28,818; Martin I. Fuchs, Reg. No. 28,508; E. Robert Yoches, Reg. No. 30,120; Barry W. Graham, Reg. No. 29,924; Susan Haberman Griffen, Reg. No. 30,907; Richard B. Racine, Reg. No. 30,415; Thomas H. Jenkins, Reg. No. 30,857; Robert E. Converse, Jr., Reg. No. 27,432; Clair X. Mullen, Jr., Reg. No. 20,348; Christopher P. Foley, Reg. No. 31,354; Roger D. Taylor, Reg. No. 28,992; John C. Paul, Reg. No. 30,413; David M. Kelly, Reg. No. 30,953; Kenneth J. Meyers, Reg. No. 25,146; Carol P. Einaudi, Reg. No. 32,220; Walter Y. Boyd, Jr., Reg. No. 31,738; Steven M. Anzalone, Reg. No. 32,095; Jean B. Fordis, Reg. No. 32,984; Barbara C. McCurdy, Reg. No. 32,120;

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FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

James K. Hammond, Reg. No. 31,964; Richard V. Burgujian, Reg. No. 31,744; J. Michael Jakes, Reg. No. 32,824; Thomas W. Banks, Reg. No. 32,719; Christopher P. Isaac, Reg. No. 32,616; Bryan C. Diner, Reg. No. 32,409; M. Paul Barker, Reg. No. 32,013; Andrew Chanho Sonu, Reg. No. 33,457; David S. Forman, Reg. No. 33,694; Vincent P. Kovalick, Reg. No. 32,867; James W. Edmondson, Reg. No. 33,871; Michael R. McGurk, Reg. No. 32,045; Joann M. Neth, Reg. No. 36,363; Gerson S. Panitch, Reg. No. 33,751; Cheri M. Taylor, Reg. No. 33,216; Charles E. Van Horn, Reg. No. 40,266; Linda A. Wadler, Reg. No. 33,218; Jeffrey A. Berkowitz, Reg. No. 36,743; Michael R. Kelly, Reg. No. 33, 921; James B. Monroe, Reg. No. 33,971; Doris Johnson Hines, Reg. No. 34,629; Allen R. Jensen, Reg. No. 28,224; Lori Ann Johnson, Reg. No. 34,498; R. Bruce Bower, Reg. No. 37,099; John Rissman, Reg. No. 33,764; M. Lawrence Oliverio, Reg. No. 30,915; Therese Hendricks, Reg. No. 30,389; Leslie I. Bookoff, Reg. No. 38,084; Michele C. Bosch, Reg. No. 40,524; Michael J. Flibbert, Reg. No. 33,234; Scott A. Herbst, Reg. No. 35,189; Leslie A. McDonell, Reg. No. 34,872; Thalia V. Warnement, Reg. No. 39,064; and Michele L. Mayberry, Reg. No. 45,644; both jointly and separately as their attorneys with full power of substitution and revocation to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith, and to receive the Letters Patent.

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GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

Please send all future correspondence concerning this application to Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P. at the following address:

Finnegan, Henderson, Farabow,
Garrett & Dunner, L.L.P.
1300 I Street, N.W.
Washington, D.C. 20005-3315

Dated: 9/3/02

By: _____
Arnold S. Milowsky, Ph.D.
Senior Patent Attorney
Wyeth

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com